Remarks

Claims 2-14 and 16-33 are pending. Claims 12 and 30 have been amended. Claim 12 has been amended to recite the correct dependency. Claim 30 has been amended to clarify the molecular weight of the polymer as being the weight average molecular weight. Support for the amendment can be found, for example, in Table 5 on page 53 of the specification, as discussed in more detail below.

Rejection Under 35 U.S.C. § 112, first paragraph

Claims 2-14 and 16-33 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly not being enabled based on the failure to recite the average molecular weight of the polymer and as not being enabled for the loss of average molecular mass of non porous materials. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

The Applicants have amended claim 30 to define the molecular weight of the polymers as the weight average molecular weight, as was actually calculated in the examples (see Table 5, on page 53) as demonstrated by the attached copy of the Declaration under 37 C.F.R. 1.132 filed in the parent case, now issued.

The Examiner is directed to Example 4, pages 53-54, describing degradation studies of 4HB *in vitro* were performed on three samples of different porosity: 0%, 50% and 80% porosity (page 54, lines 4-6). In Figure 3 and Table 6, the sample with 0% porosity is labeled "film"

(page 54, lines 12-15). This example clearly demonstrates the claimed percent loss from porous and non-porous materials.

Rejection Under 35 U.S.C. § 112, second paragraph

Claim 12 was rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to provide proper antecedent basis. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended. The units defined in the Markush group of claim 12 have antecedent basis in claim 7 comprising "unit(s) promoting chain scission." Claim 12 has been amended to depend from claim 7 as suggested by the Examiner.

Rejection Under 35 U.S.C. § 102

Claims 2-14 and 16-33 were rejected under 35 U.S.C. § 102(b or e) as anticipated by U.S. Patent No. 5,236,431 to Gogolewski et al. ("Gogolewski"), or U.S. Patent No. 6,514,515 to Williams ("Williams1") or U.S. Patent No. 6,623,749 to Williams et al. ("Williams2"). Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

Gogolewski

Gogolweski describes PHB, PHV and copolymers of PHB and PHV as preferred materials for fixation devices (column 5, lines 20-22). The Applicants attached to the response mailed January 20, 2004, references disclosing that PHB degrades very slowly *in vivo*, typically

not for 24-30 months after implantation, and that no known PHA polymer, absent modification, degrades *in vivo* in less than one year. Specifically,

1) Hazari, A. et al., *British Journal of Plastic Surgery* (1999), **52**, 653-657, states in the second paragraph on page 653 that "PHB undergoes hydrolytic degradation and is completely absorbed in 24-30 months."

2) Hazari, A. et al., *Journal of Hand Surgery* (1999), **24B**(3), 291-295, states in the third paragraph on page 291 that "PHB is non-antigenic, biocompatible, easy to handle, has good tensile strength and is completely resorbed within 24 to 30 months by hydrolytic degradation...."

3) Duvernoy, O. et al., *Thoracic Cardiovascular Surgeon* (1995), **43**, 271-274, states on page 273 that the "PHB patch was phagocytosed by macrophages and completely removed within a period of 24-30 months.

Applicants describe methods for modifying PHAs so they degrade in the desired time period. Gogolewski also does not disclose any examples of modified PHB, PHV or copolymers thereof having an average molecular mass loss of 20% to 50% over a ten week period.

Williams1

Williams1 discloses bioabsorbable biocompatible polymers selected on the basis of their physical and/or mechanical properties to correspond to the physical properties of tissues to be

regenerated or constructed. Williams1 does not teach one to make or select a *modified* polyhydroxyalkanoate with a degradation rate of less than one year to make a device.

Further, Williams1 does not suggest selecting a polymer having an average molecular mass loss of 20% to 50% over a ten week period. This relatively slow rate of molecular mass loss, *in vivo*, allows for the maintenance of polymer material properties while undergoing biodegradation.

Williams2

Williams2 discloses the development of a method for the purification of PHA, specifically to remove endotoxin from polyhydroxyalkanoates. Williams2 does not teach one to make or select a *modified* PHA with a degradation rate of less than one year.

Further, there is nothing in Williams2 to suggest making or selecting a modified PHA polymer having an average molecular mass loss of 20% to 50% over a ten week period. This relatively slow rate of molecular mass loss, *in vivo*, allows for the maintenance of polymer material properties while undergoing biodegradation.

Rejection Under 35 U.S.C. § 103

Claims 2-14 and 16-33 were rejected under 35 U.S.C. § 103(a) as obvious over U.S. Patent No. 5,236,431 to Gogolewski et al. ("Gogolewski"), U.S. Patent No. 6,514,515 to Williams ("Williams1") or U.S. Patent No. 6,623,749 to Williams et al. ("Williams2").

Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

Each of the three references cited by the Examiner under 35 U.S.C. § 103(a), has been discussed in the foregoing section, under "Rejection Under 35 U.S.C. § 102". None of Gogolewski, Williams1, or Williams2 suggests making or selecting a *modified* PHA polymer which has a controlled degradation rate of less than one year under physiological conditions and an average molecular mass loss of 20% to 50% over a ten week period. Accordingly, none of the references, alone or in combination, make obvious the claimed subject matter.

Double Patenting Rejection

Claims 2-14 and 16-33 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 27-39 of U.S. Patent No. 6,514,515 to Williams ("Williams1"). The Examiner alleges that the limitation of claim 29 of Williams1 has been achieved in the same manner as the applicants. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

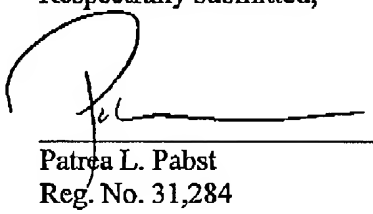
Claims 27-39 of U.S. Patent No. 6,514,515 ("Williams1") recite a device comprising a bioabsorbable biocompatible polyhydroxyalkanoate polymer, wherein the device has one or more mechanical properties equivalent to a specific tissue or tissue structure wherein the device is a tissue engineering scaffold or matrix. Claims 27-39 recite a device wherein the polymer degrades in less than two years.

Claims 2-14 and 16-33 of U.S.S.N. 10/082,954 recite a device comprising a biodegradable polyhydroxyalkanoate polymer composition that has a controlled degradation rate of less than one year under physiological conditions *and* wherein the average molecular mass loss of the polymer decreases 20% to 50% over a ten week period *in vivo*.

Claims 27-39 of Williams1 do not recite a device comprising a biodegradable polyhydroxyalkanoate composition that has a controlled degradation rate of less than one year *and* wherein the average molecular mass loss is 20% to 50% over a ten week period. Therefore, claims 2-14 and 16-33 of the present application are patentably distinct. Claims 27-39 also do not make obvious a device that has a controlled degradation rate of less than one year *and* wherein the average molecular mass loss is 20% to 50% over a ten week period and therefore claims 2-14 and 16-33 are not obvious over claims 27-39 of Williams1.

Allowance of claims 2-14 and 16-33 is respectfully solicited.

Respectfully submitted,



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COPY FILED IN USSN 10/082,854

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Simon F. Williams, David P. Martin, and Frank A. Skraly		
Serial No.:	09/535,146	Art Unit:	1714
Filed:	March 24, 2000	Examiner:	Szekely
For:	*"MEDICAL DEVICES AND APPLICATIONS OF POLYHYDROXYALKANOATE POLYMERS"*		

Assistant Commissioner for Patents
Washington, D.C. 20231

Declaration under 37 C.F.R. 1.132

Sir:

We, David P. Martin and Simon F. Williams, hereby declare that:

1. We are the inventors of the above-identified application.

2. We conducted the studies described in the application at pages 51-53, and specifically determined the molecular weights of the polymers listed in Table 5 on page 53, as follows.

Molecular weight was determined by GPC analysis. Isolated polymers were dissolved in chloroform at approximately 1 mg/mL and samples (50 μL) were chromatographed on a Waters Stryagel HT6E column at a flow rate of 1 mL chloroform per minute at room temperature using a refractive index detector. A chromatogram of relative concentration vs. elution time (i.e. elution volume) was determined for each sample. The retention time for the sample peak was determined for each unknown and a series of polystyrene standards of known weight average molecular weights obtained

from PolySciences, MA. A standard curve of log weight average molecular weight vs. peak elution time was produced for the polystyrene standards. This standard curve was linear in the molecular weight region for the unknown determinations. Comparison of the retention time of the unknown sample peak with the standard curve allowed determination of the sample molecular weight.

3. Polyhydroxybutyrate (PHB) degradation is slow and occurs in a time period of 24-30 months *in vivo* in humans and animals.

It is well known in the literature that poly-3-hydroxbutyrate (PHB) degrades very slowly when implanted in both animals and humans. There are consistent reports that complete degradation of this material takes 24-30 months:

(a) Hazari, A. et al., *British Journal of Plastic Surgery* (1999), **52**, 653-657, states in the second paragraph on page 653 that "PHB undergoes hydrolytic degradation and is completely absorbed in 24-30 months."

(b) Hazari, A. et al., *Journal of Hand Surgery* (1999), **24B**(3), 291-295, states in the third paragraph on page 291 that "PHB is non-antigenic, biocompatible, easy to handle, has good tensile strength and is completely resorbed within 24 to 30 months by hydrolytic degradation...."

(c) Duvernoy, O. et al., *Thoracic Cardiovascular Surgeon* (1995), **43**, 271-274, states on page 273 that the "PHB patch was phagocytosed by macrophages and completely removed within a period of 24-30 months.

4. I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further, that these

U.S.S.N. 09/535,146
FILED: March 24, 2000
DECLARATION UNDER 1.132

statements are made with the knowledge that willful false statements are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

David P. Martin

Simon F. Williams

Date: August 7, 2002

ATL1 #538492 v1

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